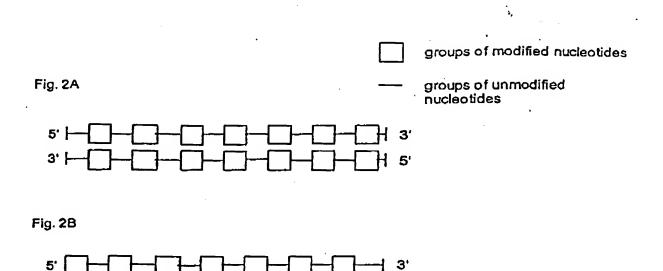
MOLECULES

Inventor: Klaus GIESE Filed: August 5, 2003

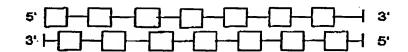
5'	3,	1st strand
3,	5'	2nd strand

MOLECULES

Fig. 2

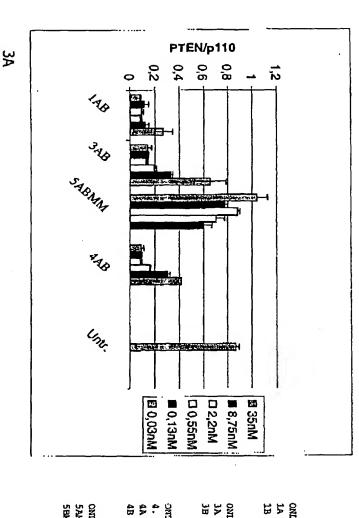






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ᅜᅜ ONLY RNA WITH 2 DEOXY AT EACH END 5'- cuccuuuuguuucugcuaacg-IT
3'-IT-gaggaaaacaaagacgauugc

ONLY RNA WITH MH2 GROWPS AT EACH 3' END AND 2 DEDXY 3 · -NH2-TT-gaggaaaacaaagacgauugc cuccuuuuguuucugcuaacg-TT-NH2

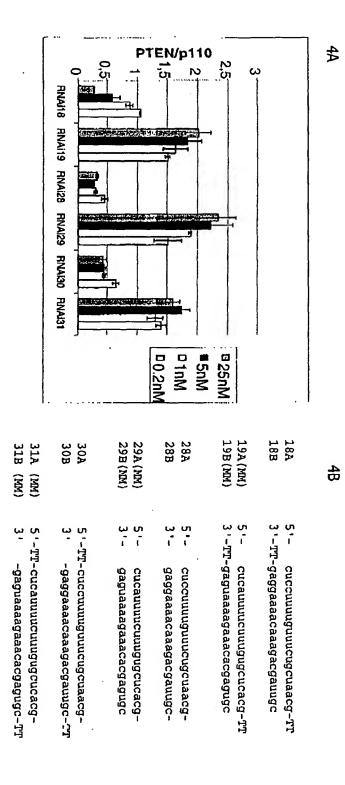
OMIY RUA WITH INVESTED ABASIC AND 2 TO 4. 16153-iB (iB at the 3' ends) 4B 3.-i8-TT-gaggaaaacaaagacgauugc cuccuuuuguuucugcuaacg-TT-iB

ONLY NNA WITH 2 DECXY AT EACH END 5AGM 5'- cucouurucuuug 5EKM 3'-TT-gagumamagamam

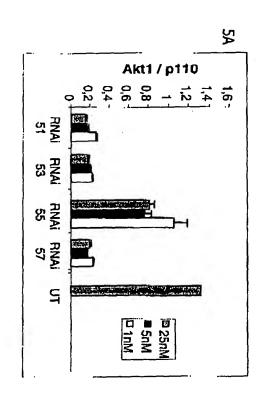
5'- cucaquincucugugcucacg-TT
3'-TT-gaguaaaagaaacacgagugc

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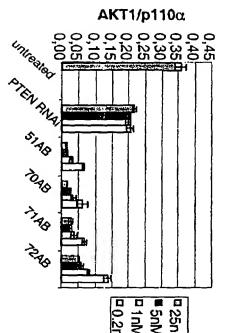
p110	PTEN		
		10 2,5 0,625 0,15 60 15 3,75 0,93	3A3B siRNA-NH2 GB53
		10 2,5 0,625 0,15 60 15 3,75 0,93	4A4B siRNA-iB GB53
		_	



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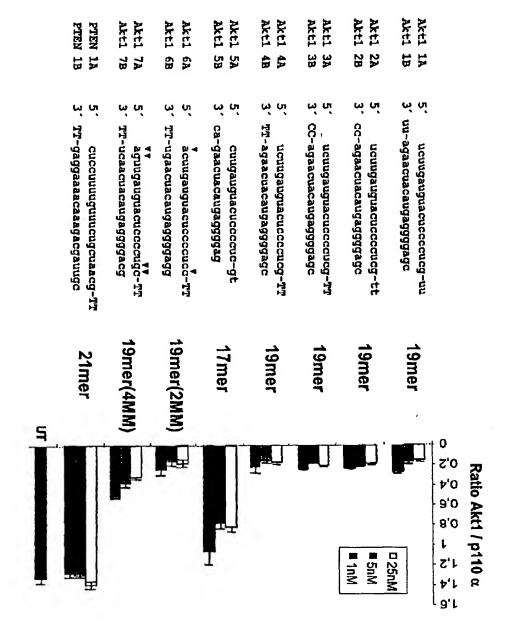
57A	55A	53A	51A
57B	55B	53B	51B
ω <u>ਯ</u> ĭ Ī	ω σ, i í	ωω	3° 1
-ucuugauguacuccccucg-TT	-cuugauguacuccccuc-gu	-ogagaecuacaugaggggage-	-ucuugauguacuccccucg-uu
CC-agaacuacaugaggggagc-	ca-gaacuacaugagggag-	co-agaacuacaugaggggage-uu	uu-agaacuacaugaggggagc-
19nt 3'seq.specific DNA	17nt 3'seq.specific RNA	19nt 3'seq.specific RNA	19nt 3'uu

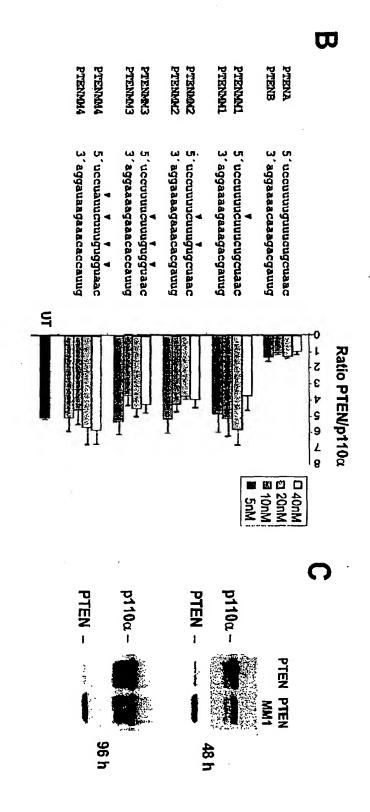


6A

	6B 19nt	6B 19nt(3'uu) 51A 5'-	-ucuugauguscucccucg-uu
25nM 5nM	51A 51B	ω σ ,	-ucuugauguscuccccucg-uu uu-agaacuacaugaggggagc-
1 Mař	19nt	(3'TT)	
0.2nM	70A	S,	-ucuugauguacuccccucg-TT
	70B	ω Ī	TT-agaacuacaugaggggagc-
	19nt	with	1MM on both sites
	71A	ن. ا	-acuugauguacuccccucc-TT
	71B	3.	TT-ugaacuacaugaggggagg-
	19nt 72A 72B	with 5'-	with 2MM on both sites 5'aguugauguacuccccugc-TT 3'- TT-ucaacuacaugagggacg-
	/ 40	i	TI-Readchardngagggargg-

MOLECULES Inventor: Klaus GIESE Filed: August 5, 2003





Inventor: Klaus GIESE Filed: August 5, 2003

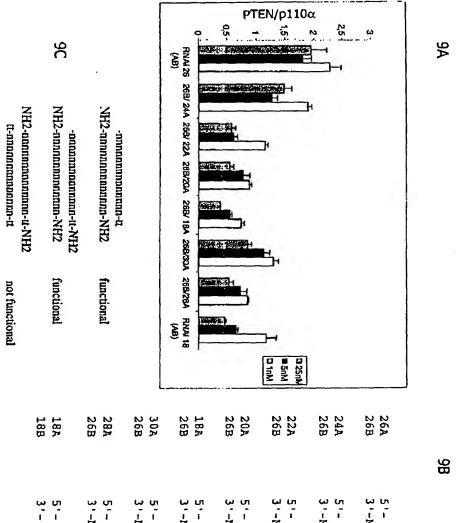
Fig. 8

82

Serum 120 18B · ω ω **Α** 30A 28A 28B 26A NH2 groups at each 3'end and 2-deoxy Only RNA with 2-deoxy at each 5' end Only RNA 79B 24B 18A 2'-0-Methyl modified with 2-deoxy at each end NH2groups at both ends AND 2-deoxy inverted abasic on both ends and 2TT

24A 5'- iB-cuccuusuguuucugcuaacg-TT-iB Tuschl 51 3'- TT-gaggamaacaaagacgauugc)'-iB-TT-gaggaaaacaaagacgauugc-iB 3.-TT-gaggaaaacaaagacgauugc 3'-NH2-TT-gaggaaaacaaagacgauugc-5'-TT-cuccuuuuguuucugcuaacg-3'-NH2-TT-gaggaaaacaaagacgauugc-NH2 5'- cuccumungunucugcuaacg-TT gaggaaaacaaagacgauugc-TT NH2-cuccuuuuguuucugcuaacg-TT-NH2 -cnccnnnndnnncndcnagcacuccuunguuucugcuaacg-IT gaggaaaacaaagacgauugccuccuuuuguuucugcuaacg-TT-NH2 88

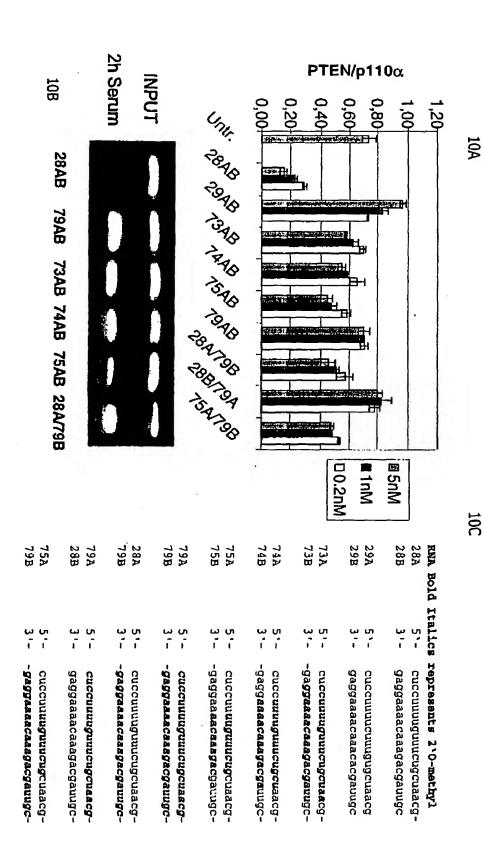
Inventor: Klaus GIESE Filed: August 5, 2003



a NITTO	nnn-1t-NH2 nnn-NH2 functional	nnn-u 1nnn-NH2 functional		268/18A 268/30A 268/28A RNA 18 (AB)		3.	н			
				8		D InM	■ 25nM			
18B	182	28A 26B	30Å 26B	26B	26B	20A	22A 26B	26B	24A	26A 26B
3'- TI-gaggaaaacaaagacgauugc	5'- cuccuungumengcuaacg-TT	5'- cuccunungunucugcuaacg- 3'-NH2-TT-gaggaaaacaaagacgaungc-NH2	5'- TT-cuccuuuuguuucugcuaacg- 3'-NH2-TT-gaggaaaacaaagacgauugc-NH2	3'-NH2-TT-gaggaaaacaaagacgauugc-NH2	3'-NH2-TT-gaggaaaaceaagacgauugc-NH2	5'- cuccumugumucugcuaacg-TT-NH2	5'- cuccuuuuguuucugcuaacg-TT-iB 3'-NH2-TT-gaggaaagacaaagacgauugc-NH2	3'-NH2-TT-gaggaaaacaaagacgauugc-NH2	5'- iB-cuccuuuguuucugcuaacg-TT-iB	5'- NH2-cuccuuuuguuucugcuaacg-TT-NH2 3'-NH2-TT-gaggaaaacaaagacgauugc-NH2

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Fig. 11

11A

110

PTEN/p110α 0,6 80 87 88 88 188 88 18 V ■ 10nM ■ 10nM □ 2.5nM

86B	83A 79B	82A 82B	81A 81B	80A 80B
₩. 5° 1	ω bī I I	ωo	ພ ຫຼ ໂ Î	ω ຫ ້
-gaggaaaacaaagacgauugc-	сиссини ндинис идсивасд	сиссиишуши <i>сидсиласд-</i> <i>даудаваясял</i> адасдашидс-	cnecuuugumengenaaeg- -gaggaaaaca aagacgauuge-	cuccuuuguuucugcuaacg- -gaggaaaacaaagacgauugc-

	2h Serum	INPUT
80AB		1
82AB		
86AB		
75A 79B		

11B

75A 79B

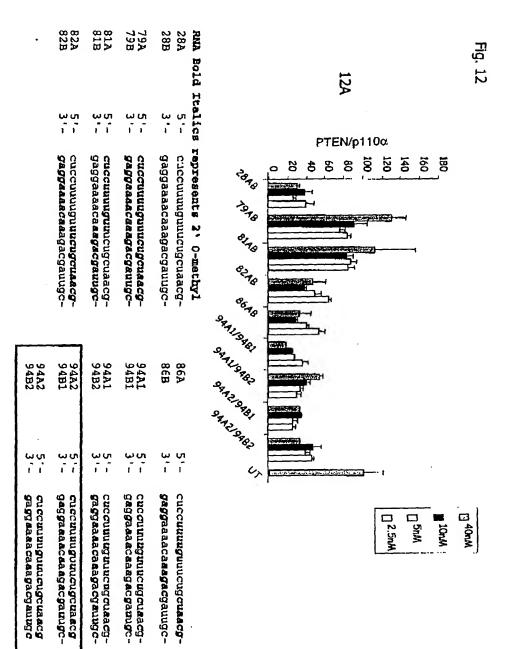
ω σ 1 1

-gaggaaaacaaagacgauugccuccuuuuguuucugcuaacg-

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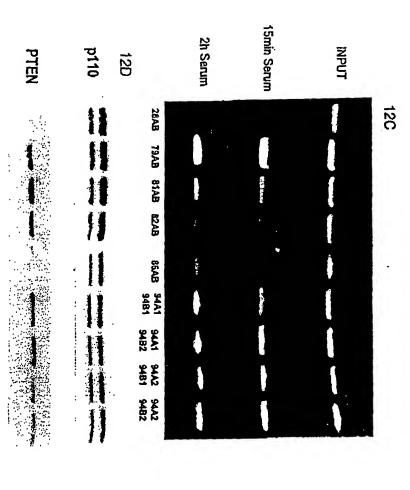
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12**B**

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Inventor: Klaus GIESE

Inventor: Klaus GIESE Filed: August 5, 2003



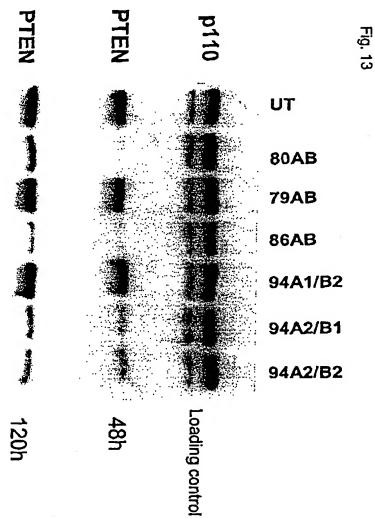
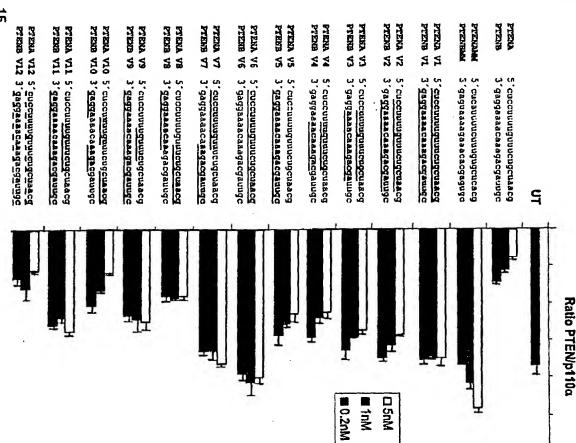


Fig. 14

PTEN PIIO UT 80AB 94A1/B2 94A2/B1 UT 80AB 94A1/B2 94A2/B1

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Filed: August 5, 2003

Inventor: Klaus GIESE

Inventor: Klaus GIESE Filed: August 5, 2003

W

		PTENB VI2 5' Gugomunugugumangagagagamaga	PTEVA VI2 PTEVB VI2	
		PTENB V15 3' GREGGREGGEGGARGACGARUGC	PTENB V15	
company on the	2h Serum	LENE A14 2. Gadatesecaredacosnicos Las estados de Constanta de Constan	PTEMB VI 4	
		PIEMB VI3 3' GROGOROSCES ROLLOS (S. 1888). S SERVIDOS CONTROLOS POR CONT	PTEMA VI.3 PTEMB VI.3	
	15min Serum	FTENA V10 3' gaggmanacamagacgaugc	PTEMA V10	
		5 cuccunungunucugenaacq	Pylana vs Pylana vs	
	INPUT	5° сиссиницицисидсивасу 3° дадувавасвандасувичес	PTENA V7 PTENB V7	
AD VI VI VO VIOVIS VIA VIS VIZ		5' спосиплядиннопасная са	PTENA VI PTENB VI	
	cuaacg	5 cuccumungunucugcuaacg 3 gaggaasacaaagacganugc	PTENA PTENB	

p110α-UT AB **%** S V10 V13 V14 V15 V12

0



Fig. 15

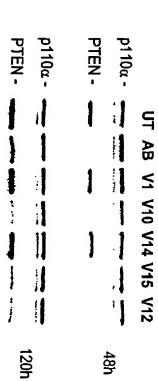
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6



Inventor: Klaus GIESE Filed: August 5, 2003

AKELA V6 AKELB V6	AKEIR VS	ALTIN VO	AKEIR V3	Aktla v2 Aktlb v2	AKEIA VI AKEIB VI
ວິດອົດມີຄວາມສວອາລີຂອດອີ ລັດຕົວຕົວຕັວສະພັດຕົວຕົວຕົວ ລັດຕົວຕົວຕົວສະພັດຕົວຕົວຕົວຕົວຕົວຕົວຕົວຕົວຕົວຕົວຕົວຕົວຕົວຕ	อมืออีธอิติดลีคอีรกีจจิด อีอกิออีออิตอิติดลีกลีอธิ. ร	ÖĞBÜĞĞĞĞÜĞN ŞOĞU ÜREĞEĞ GÖNĞOĞOĞOĞ	ວ໓໐ຽຽຽຈຈົກຂອງຊາດສະຊຽອ ເ ຄວາດວ່ອວຄວາມສອກເຄດ 5	s, agaacaacaacaccego (consolos egos (consolos egos consolos egos egos egos egos egos egos egos eg	5'ucunganguacucccucq-TT 3'TT-agaacuacaugaggggagc
	D* Akt	Akt 2	Akt 1	p110α-	
					Ę
		1			\ 2
					%
					\$
		1			UT V2 V3 V4 V5 V6
				-	V6

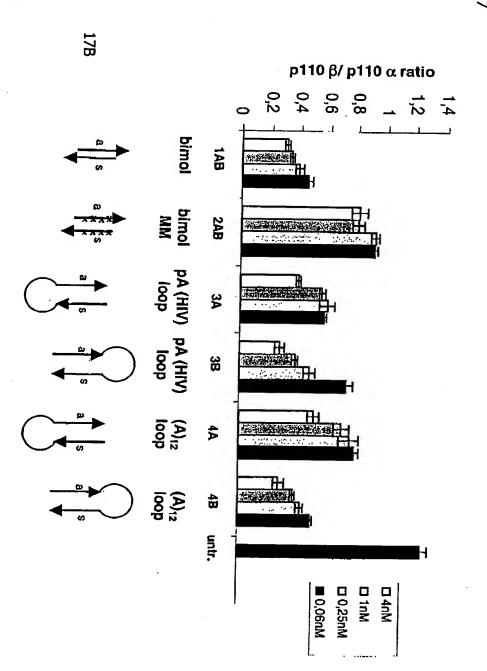
W 2h Serum INPUT V1 V2 V3 V4 V5 V6

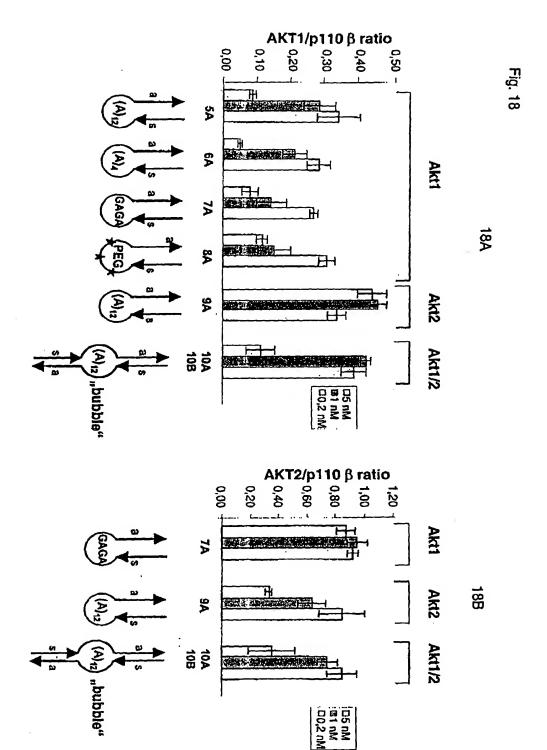
Fig. 16

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Filed: August 5, 2003

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81 golls	9110\$ V5	P110ß V4	2110β V3 :	9110B VZ 9110B VZ
Básendssocsociós Sonnsondescociós	Savingoroses de la seria (Constante de la seria del seria della se	Barchersowondari, c	openations and serior s	5'aannccaguggnucauncc 3'uuaaggucaccaaguaagg
	P*- AKI		p110a -	UT V2 V3 V4 V5 V6





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untreated

5A 6A 7A 8A 9A 10A 10A 10B

P110 α

Akt 2

P. AKI

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Filed: August 5, 2003

Fig. 19